BEST AVAILABLE COPY

Application No. Amendment Dated Reply to Office Action of

10/088,352 27th Jur e 2005 28th November 2005

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

(currently amended) A compound of formula (I) 1.

$$\mathbb{R}^{3}$$
 \mathbb{R}^{1}
 \mathbb{R}^{4}
 \mathbb{R}^{8}
 \mathbb{R}^{7}
 \mathbb{R}^{6}
 \mathbb{R}^{5}
 \mathbb{R}^{9}
 \mathbb{R}^{9}
 \mathbb{R}^{1}
 \mathbb{R}^{9}
 \mathbb{R}^{1}
 \mathbb{R}^{1}
 \mathbb{R}^{1}
 \mathbb{R}^{2}
 \mathbb{R}^{3}

or a salt, or phosphate ester, or amide thereof;

where X is O, or S, S(O) or S(O); or NR 10 where R 10 is hydrogen or C $_{1-6}$ alkyl;

 R^{5} is a group OR^{11} , $NR^{12}R^{13}$ or SR^{11} where R^{11} , R^{12} and R^{13} are independently selected from hydrogen, optionally substituted hydrocarbyl where optional substituents are functional groups. or optionally substituted heterocyclic groups where optional substituents are functional groups or hydrocarbyl, and R¹² and R¹³ may additionally form together with the nitrogen atom to which they are attached, an optionally substituted aromatic or non-aromatic heterocyclic ring which may contain further heteroatoms:[[,]]

 R^6 and R^7 are independently selected from hydrogen or hydrocarbyl;

 R^{8} and R^{9} are independently selected from hydrogen, halo, $C_{1\text{--}4}$ alkyl, $C_{1\text{--}4}$ alkoxy.

 C_{1-4} alkoxymethyl, di $(C_{1-4}$ alkoxy)methyl, C_{1-4} alkanoyl, trifluoromethyl, cyano, amino, C_{2-5} alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms[[,]] selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated, linked via a ring carbon or nitrogen atom, or unsaturated, linked via a ring carbon atom, [[,]] and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C_{2-4} alkanoyl, C_{1-4} alkanoylamiro, C_{1-4} alkoxycarbonyl, C_{1-4} alkylsulphanyl, C_{1-4} alkylsulphinyl, $C_{1\rightarrow a}$ alkylsulphonyl, carbamoyl. N- $C_{1\rightarrow a}$ alkylcarbamoyl, N,N-dl($C_{1\rightarrow a}$ alkyl)carbamoyl,

10/088,352 27th Jur e 2005 28th November 2005

aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperaz_inyl, piperidinyl, imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl:[[,]] and

- R^1 , R^2 , R^3 , R^4 are independently selected from halogeno, cyano, nitro, $C_{1:3}$ alkylsulphanyl, $-N(OH)R^{14}[[.]]$ wherein R^{14} is hydrogen[[,]] or $C_{1:3}$ alkyl, [[,]] or $R^{16}X^1$ wherein X^1 represents a direct bond, -O-, $-CH_2$ -, -OC(O)-, -C(O)-, -S-, -SO-, $-SO_2$ -, $-NR^{17}C(O)$ -, $-C(O)NR^{18}$ -, $-SO_2NR^{19}$ -, $-NR^{20}SO_2$ or $-NR^{21}$ -, wherein R^{17} , R^{18} , R^{19} , R^{20} and R^{21} each independently represents hydrogen, $C_{1:3}$ alkyl or $C_{1:3}$ alkoxy $C_{1:3}$ alkyl, [[,]] and R^{16} is hydrogen, optionally substituted heterocyclyl or optionally substituted alkoxy selected from one of the following twenty-two groups:
- 1) hydrogen or C_{1-5} alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydrogy, oxiranyl, fluoro, chloro, bromo, amino, C_{1-5} alkyl, and trifluoromethyl;
- 2) -R³X²C(O)R²²; wherein X² represents -O- or -NR²³-, in which R²³ represents hydrogen,

 C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²² represents C₁₋₃alkyl, -NR²⁴R²⁵ or -OR²⁸, wherein R²⁴, R²⁵

 and R²⁶ which may be the same or different each represents hydrogen, C₁₋₅alkyl,

 hydroxyC₁₋₅alkyl or C₁₋₃alkoxyC₂₋₃alkyl;
- 3) -R^bX³R²⁷; wherein X³ represents -O-, C(O) -S-, -SO-, -SO₂-, -OC(O)-, -NR²⁸C(O)-, -NR²⁸C(O)-, -NR²⁸C(O)-, -C(O)NR²⁹-, -C(O)DNR²⁹-, -SO₂NR³⁰-, -NR³¹SO₂- or -NR³²-, wherein R²⁸, R²³, R³⁰, R³¹ and R³² each independently represents hydrogen, C₁₋₃alkyl, hydroxy C₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and R²⁷ represents hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclopexyl, phenyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₆alkyl group may bear 1, 2 or 3 substituents selected from oxo, hydroxy, halogeno, cyclopropyl, amino, C₁₋₄alkylamino, C₁₋₄alkylamino, C₁₋₄alkylamino, C₁₋₄alkylamino, C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C₁₋₄cyanoalkyl, C₁₋₄alkyl, C₁₋₄alkylamino dl(C₁₋₄alkyl)amino, C₁₋₄alkylaminoC₁₋₄alkyl, C₁₋₄alkyl)aminoC₁₋₄alkyl, C₁₋₄alkylaminoC₁₋₄alkyl, C₁₋₄alkyl, C₁₋₄alkyl, C₁₋₄alkyl, C₁₋₄alkyl)aminoC₁₋₄alkyl, C₁₋₄alkyl, C₁₋₄alkyl, C₁₋₄alkyl, C₁₋₄alkyl)aminoC₁₋₄alkoxy and a group droup, an aryl group or a 5-6-nembered saturated or unsaturated heterocyclic group with 1-2 group, an aryl group or a 5-6-nembered saturated or unsaturated heterocyclic group with 1-2

Application No. Application No.
Amendment Dated
Reply to Office Action of

10/088,352 27th Jur e 2005 28th November 2005

heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo or C₁₋₄alkyl;

- 4) -R°X4R° X6R35; wherein X4 and X1 which may be the same or different are each -O-, C(O), -S-, -SO-, -SO₂-, -NR³⁶C(O)-, -NR³⁶C(O)O-, -C(O)NR³⁷-, -C(O)ONR³⁷-, -SO₂NR³⁸-, -NR³⁹SO₂- or -NR⁴⁰-, wherein R³⁵, R³⁷, R³⁸, R³⁹ and R⁴⁰ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and R³⁵ represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or
- C₁₋₃alkoxyC₂₋₃alkyl; 5) R⁴¹; wherein R⁴¹ is a 4-6-membered cycloalkyl or saturated heterocyclic ring, linked via carbon or nitrogen, with 1-2 heteroatoms, selected independently from O, S and N, which cycloalkyl or heterocyclic group may bear 1 or 2 substituents selected from exe, hydroxy, halogeno, cyano, C₁₋₄alkyl, hydroхуС₁₋₄alkyl, cyanoС₁₋₄alkyl, cyclopropyl,

 C_{1-4} alkylsulphonyl C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, carboxamido, C_{1-4} aminoalkyl, C_{1-4} alkylamino, $\underline{\text{di}(C_{1-4}\text{alkyl})\text{amino}, C_{1-4}\text{alkyl}\underline{\text{amino}}C_{1-4}\text{alkyl}, C_{1-4}\text{alkanovl}, \underline{\text{di}(C_{1-4}\text{alkyl})\text{amino}}C_{1-4}\text{alkyl},}$

 C_{14} alkylamino C_{14} alkoxy, di $(C_{14}$ alkyl)amino C_{14} alkoxy nitro, amino, C_{14} alkoxy,

C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, -C(O)NR⁴³R⁴⁴, -NR⁴⁵C(O)R⁴⁶, wherein R⁴³, R⁴⁴, R⁴⁵ and R⁴⁶, which may be the same or different, each represents hydrogen, C₁₋₄alkyl,

hydroxyC₁₋₄alkyl or C₁₋₃alkoxyC₂: alkyl) and a group -(-O-)_i(C₁₋₃alkyl)_oringD, wherein f is 0 or 1, g is 0 or 1 and D is a cyclic group selected from C₃₋₈cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group vith 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl;

6) -RdR41; wherein R41 is as defined hereinbefore;

7) - ReR41; wherein R41 is as defined hereinbefore;

8) -Rf R41; wherein R41 is as defined hereinbefore;

9) R⁴²; wherein R⁴² represents (1 phenyl group or a 5-6-membered aromatic heterocyclic group, linked via carbon or nitrogen, with 1-3 heteroatoms selected from O, N and S, which phenyl or aromatic heterocyclic group may carry up to 5 substituents selected from hydroxy, nitro, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C1-hydroxyalkoxy, oxo, cyano(21-alkyl, cyclopropyl, C1-alkylsulphonylC1-alkyl, C_{1-4} alkoxycarbonyl, di(C_{1-4} alkyl)amino, C_{1-4} alkylamino C_{1-4} alkyl, C_{1-4} alkanoyl, $\underline{\text{di}(C_{14}\text{alkyl})\text{amino}C_{14}\text{alkyl},\ C_{1-|\mathbf{alkyl}|\mathbf{amino}C_{14}\text{alkoxy},\ \mathbf{di}(C_{14}\text{alkyl})\text{amino}C_{14}\text{alkoxy},\ \mathbf{carboxy},}$ carboxamido, trifluoromethyl, cyano, -C(O)NR⁶⁹R⁷⁰, -NR⁷¹C(O)R⁷², wherein R⁶⁹, R⁷⁰, R⁷¹ and R⁷². which may be the same or different, each represents hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and a group -(-O-)₁(C₁₋₄alkyl)₀ringD, wherein f is 0 or 1, q is 0 or 1 and ring D is a cyclic group selected from Cacycloalkyl, aryl or 5-6-membered saturated or unsaturated

10/088,352 27th June 2005 28th November 2005

heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl;

- 10) -R9R42; wherein R42 is as defined hereinbefore;
- 11) -RhR42; wherein R42 is as defined hereinbefore;
- 12) -RIR42; wherein R42 is as defined hereinbefore;
- 13) -RIX⁶R⁴²; wherein X⁶ represents: -O-, -C(O)-, -S-, -SO-, -SO₂-, -OC(O)-, -NR⁴⁷C(O)-,
- -C(O)NR⁴⁸-, C(O)ONR⁴⁸-, -SO₂NR⁴³-, -NR⁵⁰SO₂- or -NR⁵¹-, wherein R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰ and R⁵¹ each independently represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and
- R42 is as defined hereinbefore; 14) -R^kX⁷R⁴²; wherein X⁷ represents -O-, C(O), -S-, -SO-, -SO₂-, -NR⁷³C(O)-, -C(O)NR⁷⁴-,
- C(O)ONR⁷⁴-, -SO₂NR⁷⁵-, -NR⁷⁶SO₂- or -NR⁷⁷-, wherein R⁷³, R⁷⁴, R⁷⁵, R⁷⁶ and R⁷⁷ each
- independently represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and R⁴² is
- 15) -R^mX⁸R⁴²; wherein X⁸ represents -O-, -C(O)-, -S-, -SO-, -SO₂-, -NR⁵⁷C(O)-, -C(O)NR⁵⁸-,
- -SO₂NR⁵⁹-, -NR⁶⁰SO₂- or -NR⁶¹-, wherein R⁵⁷, R⁵⁸, R⁵⁹, R⁶⁰ and R⁶¹ each independently
- represents hydrogen, Ctalkyl, hydroxyCtalkyl or CtalkoxyCalalkyl, and R42 is as defined
- 16) -R"X⁹R"¹R⁴²; wherein X⁹ represents -O-, -C(O)-, -S-, -SO-, -SO₂-, -NR⁶²C(O)-, -C(O)NR⁶³-, hereinbefore:
- C(O)ONR⁶³-, -SO₂NR⁶⁴-, -NR⁶⁵S₁O₂- or -NR⁶⁶-, wherein R⁶², R⁶³, R⁶⁴, R⁸⁵ and R⁶⁶ each
- independently represents hydroclen, C_{1-3} alkyl, hydroxy C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{42} is as defined hereinbefore;
- 17) -R^pX⁹-R^pIR⁴¹; wherein X⁹ and R⁴¹ are as defined hereinbefore;
- 18) C₂₋₅alkenyl which may be ur substituted or which may be substituted with one or more groups selected from hydroxy, f.uoro, amino, C14alkylamino,
- N,N-di(C₁₋₄alkyl)amino, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl and
- N,N-di(C_{1-s}alkyl)aminosulphonyl;
- 19) C₂₋₅alkynyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C1-alkylamino,
- N,N-di(C₁₋₄alkyl)amino, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl and
- N,N-di(C₁₋₄alkyl)aminosulphon'/l;
- 20) -R¹X⁹R^rR⁴¹: wherein X⁹ and R⁴¹ are as defined hereinbefore;
- 21) -R"X" R"R41; wherein X and R41 are as defined hereinbefore; and
- 22) $R^{\nu}R^{67}(R^{\nu})_{a}(X^{9})_{c}R^{68}$; wherein X^{9} is as defined hereinbefore, q is 0 or 1, r is 0 or 1, and R^{67} is
- a Ctaalkylene group or a cyclic group selected from cyclopropyl, cyclobutyl, cyclopentylene,

Application No.

Amendment Dated
Reply to Office Action of
27th Jur e 2005
28th November

10/088,352 28th Nevember 2005

cyclohexylene or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which Ct-salkylene group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C. alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C14cyanoalkyl, C14alkyl, C14hydroxyalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} ilkylsulphonyl C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, C_{1-4} aminoalkyl, $C_{1.4}$ alkylamino, di($C_{1.4}$ alkyl)amino, $C_{1.4}$ alkylamino $C_{1.4}$ alkyl, di($C_{1.4}$ alkyl)amino $C_{1.4}$ alkyl, C_{1-1} alkylamino C_{1-1} alkoxy, di $(C_{1-1}$ alkyl)amino C_{1-1} alkoxy and a group -(-O-) $_{1}$ (C_{1-1} alkyl) $_{0}$ ringD, wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from C₃₋₅cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl; and R⁶⁸ is hydrogen, C₁₋₃alkyl, or a cyclic group selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C₁₋₄cyanoalkyl, $\underline{C_{1.4}} \underline{alkyl}, \underline{C_{1.4}} \underline{hydroxyalkyl}, \underline{C_{1.4}} \underline{alkoxy}, \underline{C_{1.4}} \underline{alkoxy} \underline{C_{1.4}} \underline{alkyl}, \underline{C_{1.4}} \underline{alkyl},$ C_{1-4} alkoxycarbonyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{1-4} alkylamino C_{1-4} alkyl, $\underline{\text{di}(C_{1-4}\text{alkyl})\text{amino}C_{1-4}\text{alkyl},\ C_{1-4}\text{alkyl}\text{amino}C_{1-4}\text{alkoxy},\ \underline{\text{di}(C_{1-4}\text{alkyl})\text{amino}C_{1-4}\text{alkoxy}}\text{ and a group}}$ -(-O-)_t(C₁₋₄alkyl)_aringD, wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from C₃₋₆cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C14alkyl; and wherein R^a, R^b, R^b, R^c, R^c, R^c, R^d, R^g, R^l, Rⁿ, Rⁿ, R^p, R^p, R^r, R^r, R^r, R^v and R^{v'} are independently

selected from C_{1-x}alkylene groups optionally substituted by one or more substituents selected from hydroxy, halogeno, amino,

R^a R^b, R^k and R^t are independently selected from C₂₋₈alkenylene groups optionally substituted by one or more substituents selected from hydroxy, halogeno, amino, and Rt may additionally be a

RI, RI, Rm and Ru are independently selected from by C2-8alkynylene groups optionally substituted by one or more substituents selected from hydroxy, halogeno, amino; wherein a phosphate ester is a derivative of a hydroxy group present on one or more of R1, R2,

wherein functional group refers to reactive substituents selected from nitro, cyano, halo, oxo, $= CR^{78}R^{79}, C(O)_{c}R^{77}, OR^{77}, S(O)_{c}R^{77}, NR^{78}R^{79}, C(O)NR^{78}R^{79}, OC(O)NR^{78}R^{79}, = NOR^{77},$

10/088,352 27th Jure 2005 28th November 2005

 $-NR^{77}C(O)_{\nu}R^{78}, -NR^{77}CONR^{78}R^{79}, -N = CR^{78}R^{79}, S(O)_{\nu}NR^{78}R^{79} \text{ or } -NR^{77}S(O)_{\nu}R^{78} \text{ where } R^{77}, R^{78}$ and R79 are independently selected from hydrogen, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted C₁₋₁₀alkoxy, or R⁷⁸ and R⁷⁹ together form an optionally substituted ring which optionally contains further heteroatoms such as oxygen, nitrogen, S, S(O) or S(O)2, where x is an integer of 1 or 2, y is 0 or an integer of 1-3; and where optional substituents for hydrocarbyl, heterocyclyl or C₁₋₁₀alkoxy groups R⁷⁷, R⁷⁸ and R⁷⁹ as well as rings formed by R⁷⁸ and R⁷⁹ are halo, perhaloC₁₋₁₀alkyl, mercapto, thioC₁₋₁₀alkyl, hydroxy. carboxy, C₁₋₁₀alkoxy, heteroaryl, heteroaryloxy, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkenyl, C_{3-10} cycloaikynyl, C_{2-10} alkenyloxy, C_{2-10} alkynyloxy, C_{1-10} alkoxy C_{1-10} alkoxy, aryloxy where the aryloxy group may be substituted by halo, nitro or hydroxy, cyano, nitro, amino, mono- or di-C₁₋₁₀alkyl amino, oximino or S(O), R90 where y is as defined above and R90 is a C1-10 alkyl; and wherein hydrocarbyl is selected from C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, aryl, arC₁₋₁₀alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl or C_{3-10} cycloalkynyl; or C_{1-10} alkyl, C_{2-10} alkenyl or C_{2-10} alkynyl substituted with aryl, arC₁₋₁₀alkyl, 12₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkenyl or C₃₋₁₀cycloalkynyl; or an aryl, heterocyclyl, C₁₋₁₀alkoxy, arC₁₋₁₀alkyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkenyl or C₃₋₁₀cycloalkynyl substituted with C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl or C₁₋₁₀alkoxy...

(cancelled) 2-6.

(currently amended) A compound-of-formula (IA) 7.

$$\mathbb{R}^{1}$$
 \mathbb{R}^{1} \mathbb{R}^{1} \mathbb{R}^{2} \mathbb{R}^{3} \mathbb{R}^{4} \mathbb{R}^{4} \mathbb{R}^{4}

according to claim 1, or a salt, or phosphate ester or amide thereof; wherein where X is O, or S, S(O) or S((1))2, NH or NR¹⁰ where R¹⁰ is hydrogen or C_{1 s}alkyl;

10/088,352 27th Jure 2005 28th November 2005

R⁵-is-a group OR¹¹, NR¹²R¹³-or-SR¹¹: where R¹¹, R¹²-and R¹³-are-independently selected from hydrogen, eptionally substituted hydrocarbyl-or eptionally substituted heterocyclic-groups, and R⁴² and R⁴³ may additionally form-tegother with the nitrogen atom to which they are attached, an arematic or non-arematic heterocyclic ring which may contain further heteroatems, R⁸-and R⁹-are-independently selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄alkoxy, C_{1-4} alkoxymethyl, di(C_{1-4} alkoxy)methyl, C_{1-4} alkanoyl, trifluoremethyl, cyano, amino, C_{2-6} alkenyl, C₂₋₆alkynyl, a phonyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected-independently from O, S and N, which heterocyclic-group-may be arematic or non-arematic and may be saturated, linked-via-a ring carbon or nitregen-atom, or uncaturated, linked via a ring carbon atom, and which phonyl, benzyl or heterocyclic group may bear-on-one or more ring earbon atoms up to 5-substituents-selected-from hydroxy, halogeno, C_{1-3} alkyl, C_{1-3} alkexy, C_{1-3} alkanoylexy, trifluoromethyl, cyano, amino, nitro, C_{2-4} alkanoylexy, trifluoromethyl, cyano, amino, a G_{14} alkaneylamine; G_{14} alkexycarbenyl, G_{14} alkylculphanyl, G_{14} alkylculphinyl, G_{14} alkylculphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl,

 $N_{+}N-di(G_{1-4}alkyl)$ carbamoyl, aminc sulphonyl, $N-G_{1-4}alkyl$ aminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, '2₄₋₄alkylsulphonylamino, and a-saturated heterocyclic group selected from morpholine, thioms rpholine, pyrrolidinyl, piperazinyl, piperidinyl, imidazolidinyl and pyrazolidinyl, which saturated he erocyclic group-may bear-1 or 2 substituents selected from exe, hydroxy, halegene, C_{4-3} alkyl, C_{4-3} alkexy, C_{4-3} alkaneylexy, triflueremethyl, cyane, amine, nitro-and C1-4alkexycarbonyl, and

 R^1 , R^2 , R^3 , R^4 are independently selected from, halo, cyano, nitro, trifluoromethyl, $C_{1\cdot3}$ alkyl, -NR¹⁴R¹⁵, wherein R¹⁴ and R¹⁶, which may be the same or different, each represents hydrogen or C₁₋₃alkyl, or -X¹R¹⁶, wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR¹⁷CO-, -CONR¹⁸-, -SO₂NR¹⁹-, -NR²⁰SO₂- or -NR²¹-, wherein R¹⁷, R¹⁸, R¹⁸, R²⁰ and R^{21} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{18} is selected from one of the following seventeen groups:

- 1') hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro or amino:[[,]]
- 2') C_{1-5} alkyl X^2COR^{22} ; wherein X^2 represents -O- or -NR²³-[[,]] in which R²³ represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{22} represents C_{1-3} alkyl, $-NR^{24}R^{25}$ or $-OR^{26}$, wherein R^{24} , R^{25} and R^{26} which may be the same or different each represents hydrogen, $C_{1\cdot 2}$ alkyl or
- 3') C_{1-5} alky IX^3R^{27} ; wherein X^3 represents -O-, -S-, -SO-, -SO₂-, -OCO-, -NR²⁸CO-, -CONR²⁹-, -SO₂NR³⁰-, -NR³¹SO₂- or -NR¹²-, wherein R²⁸, R²⁹, R³⁰, R³¹ and R³² each independently

10/088,352 27th Jur e 2005 28th November 2005

represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and R²⁷ represents hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms[[,]] selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and $C_{1\text{--}4}$ alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{14} alkyl, C_{14} hydroxyalkyl and

- 4') C_{1-5} alkyl X^4 C_{1-5} alkyl X^5 R^{35} ; wherein X^4 and X^5 which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR³⁶CO-, -C:ONR³⁷-, -SO₂NR³⁸-, -NR³⁸SO₂- or -NR⁴⁰-, wherein R³⁶, R³⁷, R^{38} , R^{39} and R^{40} each independently represents hydrogen, $C_{1\text{--}3}$ alkyl or $C_{1\text{--}3}$ alkoxy $C_{2\text{--}3}$ alkyl, and R³⁵ represents hydrogen or C₁₋₃alkyl;
- 5') R⁴¹; wherein R⁴¹ is a 5-6-membered saturated heterocyclic group, linked via carbon or nitrogen, with 1-2 heteroatoms[[,]] selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{14} hydroxyalkyl, C_{14} alkoxy, C_{14} alkoxy C_{14} alkyl and C_{14} alkylsulphonyl C_{14} alkyl;
- 6') C₁₋₅alkyIR⁴¹; wherein R⁴¹ is as defined hereinbefore;
- 7') C₂₋₅alkenylR⁴¹; wherein R⁴¹ is as defined hereinbefore;
- 8') C_{2-5} alkynyl \mathbb{R}^{41} ; wherein \mathbb{R}^{41} is as defined hereinbefore;
- 9') R⁴²; wherein R⁴² represents a phenyl group or a 5-6-membered aromatic heterocyclic group, linked via carbon or nitrogen, with 1-3 heteroatoms selected from O, N and S, which phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino, C_{1-4} hydroxyalkoxy, carboxy, trifluoromethyl, cyano, -CONR⁴³R⁴⁴ and -NR 45 COR 46 , wherein R 43 , R 44 , R 45 and R 46 , which may be the same or different, each represents hydrogen, C1-4alkyl or C1-3alkox/C2-3alkyl;
 - 10') C₁₋₅alkylR⁴²; wherein R⁴² is as defined hereinbefore;
 - 11') C₂₋₅alkenylR⁴²; wherein R⁴⁷ is as defined hereinbefore;
 - 12') C₂₋₅alkynylR⁴²;wherein R⁴² is as defined hereinbefore;
 - 13') C_{1-5} alkyl X^8R^{42} ; wherein X^6 represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁷CO-, -CONR⁴⁸-, -SO $_2$ NR 49 -, -NR 50 SO $_2$ - or -NR $^{5'}$ -, wherein R 47 , R 48 , R 49 , R 50 and R 51 each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{42} is as defined hereinbefore; 14') C_{2-5} alkenyl X^7 R^{42} ; wherein X^7 represents -O-, -SO-, -SO₂-, -NR⁵²CO-, -CONR⁵³-, -SO₂NR⁵⁴-, -NR⁵⁵SO₂- or -NR⁵⁶-, wherein R⁵², R⁵³, R⁵⁴, R⁵⁵ and R⁵⁶ each independently represents hydrogen, C_{1-3} alkyı or C_{1-3} alkoxy C_{2-3} alkyl, and R^{42} is as defined hereinbefore;

10/088;352 27th Jur e 2005 28th November 2005

- 15') $C_{2\cdot5}$ alkynyl X^8R^{42} ; wherein X^8 represents -O-, -S-, -SO-, -SO₂-, -NR⁵⁷CO-, -CONR⁵⁸-, -SO₂NR⁵⁹-, -NR⁶⁰SO₂- or -NR⁶¹-, wherein R⁵⁷, R⁵⁸, R⁵⁹, R⁸⁰ and R⁶¹ each independently represents hydrogen, $C_{1\cdot3}$ alkyl or $C_{1\cdot3}$ alkoxy $C_{2\cdot3}$ alkyl, and R⁴² is as defined hereinbefore; 16') $C_{1\cdot3}$ alkyl $X^8C_{1\cdot3}$ alkyl X^{42} ; wherein X^9 represents -O-, -S-, -SO-, -SO₂-, -NR⁶²CO-, -CONR⁶³-, -SO₂NR⁸⁴-, -NR⁶⁵SO₂- or -NR⁶⁶-, wherein R⁶², R⁶³, R⁶⁴, R⁶⁵ and R⁶⁵ each independently represents hydrogen, $C_{1\cdot3}$ alkyl or $C_{1\cdot3}$ alkoxy $C_{2\cdot3}$ alkyl, and R⁴² is as defined hereinbefore; and 17') $C_{1\cdot3}$ alkyl $X^9C_{1\cdot3}$ alkyl X^{41} ; wherein X^9 and X^{41} are as defined hereinbefore; and R⁶ and R⁷ are hydrogen or $C_{1\cdot4}$ alkyl.
 - 8. (currently amended) A compound according to claim 7, or a salt or phosphate ester, thereof wherein R⁶ and R⁷ are hydrogen.
 - 9. (cancelled)
 - 10. (currently amended) A compound according to claim $\underline{1}$ [[6]] or a salt or phosphate ester thereof, wherein R^5 is selected from a group OR^{11} where R^{11} is hydrogen or $C_{1.4}$ alkyl; or a group $NR^{12}R^{13}$ where one of R^{12} or R^{13} is hydrogen and the other is optionally substituted $C_{1.6}$ alkyl, optionally substituted aryl or optionally substituted heterocyclyl, or R^{12} and R^{13} together with the nitrogen atom to which they are attached form a heterocyclic ring.
 - 11. (previously presented) A compound according to claim 10, which is a phosphate ester of a compound of formula (I).
 - 12. (currently amended) A method for preparing a compound of formula (I) as defined in claim 1 which method comprises reacting a compound of formula (II)

10/088,352 27th Jure 2005 28th November 2005

(11)

where X, R⁸ and R⁹ are as defined in claim 1, R¹, R², R³, R⁴ are groups R¹, R², R³, R⁴ as defined in claim 1 respectively; and R^{B5} is a leaving group, with a compound of formula (III)

where R^6 are R^7 are as defined in claim 1 and R^{5} is a group R^5 as defined in claim 1.

- (cancelled) 13.
- (currently amended) A method for treating colorectal or breast cancer in a warm blooded animal, in need of such treatment, which comprises administering to said animal an effective amount of a compound of formula (I), or a salt[[,]] or phosphate ester, or amide thereof.
- (currently amended) A pharmaceutical composition comprising a compound of formula (I) as defined in claim 1, or a salt[[,]] or phosphate ester, or amide thereof, in combination with a pharmaceutically acceptable carrier.
- (currently amended) A compound according to claim 10, or a salt[[,]] or phosphate ester 16. er amide thereof; where

R⁵ is a group OR¹¹, NR¹²R¹³ or SR¹¹ where R¹¹ is hydrogen or C₁₋₄alkyl, and where one of R¹² and R^{13} is hydrogen and the other is $C_{1\text{-}8}$ alkyl optionally substituted with one or more groups selected from hydroxy, trifluoron ethyl, C_{1-3} alkoxy, cyano, amino, mono- or di- C_{1-4} alkylamino, C₁-alkylthio, C₃-cycloalkyl or heterocyclyl optionally substituted with C₁-alkyl; or one of R¹² and R^{13} is hydrogen and the other is a heterocyclic group as well as dioxides thereof, $C_{3\text{-}6}$ cycloalkyl or a phenyl group any of which may be substituted with one or more groups selected from halo, nitro, C_{1-4} alkył or C_{1-4} alkoxy, an ł R^{12} and R^{13} may additionally form together with the nitrogen atom to which they are attached, morpholine or piperidine;[[,]]

R⁶ and R⁷ are independently selected from hydrogen or C₁₄alkyl;

 R^8 and R^9 are independently selected from hydrogen, halo, $C_{1^{-4}}$ alkoxy, trifluoromethyl, cyano or phenyl.

10/088,852 27th June 2005 28th November 2005

- (currently amended) A compound according to claim 16, or a salt or phosphate ester 17. thereof, wherein X is NH or O.
- (currently amended) A compound according to claim 16, or a salt or phosphate ester 18. thereof, wherein

 R^2 is halo, cyano, nitro, trifluoromethyl, C_{1-3} alkyl, -NR¹⁴R¹⁵, wherein R¹⁴ and R¹⁵, which may be the same or different, each represents hydrogen or C_{1-3} alkyl, or a group $-X^1R^{16}$ where X^1 is oxygen and R18 is a group (1); as defined in claim 6,

 R^3 is a group $-X^1R^{16}$ where X^1 is exygen and R^{16} is a group selected from group (1), (3), (6) and (10); as defined in claim-6

and R4 is hydrogen, halo, C1-4alkyl, or C1-4alkoxy;

wherein group (1) is hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, oxiranyl, fluoro, chloro, bromo, amino, C1-3alkyl and trifluoromethyl;

group (3) is -R^bX³R²⁷; wherein X² represents -O-, C(O) -S-, -SO-, -SO₂-, -OC(O)-, -NR²⁸C(O)-, -NR²⁸C(O)O-, -C(O)NR²⁹-, C(O)()NR²⁹-, -SO₂NR³⁰-, -NR³¹SO₂- or -NR³²- wherein R²⁸, R²⁹, R³⁰, R31 and R32 each independently represents hydrogen, C1-3alkyl, hydroxy C1-4alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and R²⁷ represents hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phanyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-s}alkyl group may bear 1, 2 or 3 substituents selected from oxo, hydroxy, halogeno, cyclopropyl, amino, C₁₋₄alkylamino, C₁₋₄alkanovldi-C₁₋₄alkylamino, C₁₋₄alkylthio, C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C₁₋₄cyanoalkyl, C₁₋₄alkyl, C_{14} hydroxyalkyl, C_{14} alkoxy, C_{14} alkoxy C_{14} alkyl, C_{14} alkylsulphonyl C_{14} alkyl, C_{14} alkoxycarbonyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{1-4} alkylamino C_{1-4} alkyl, $\underline{\text{di}(C_{1\!-\!4}\text{alkyl})\text{amino}C_{1\!-\!4}\text{alkyl},\ C_{1\!-\!4}\text{alkyl}\text{amino}C_{1\!-\!4}\text{alkoxy},\ \underline{\text{di}(C_{1\!-\!4}\text{alkyl})\text{amino}C_{1\!-\!4}\text{alkoxy}\ \text{and}\ \text{a}\ \text{group}}$ $-(-O-)_f(R^b)_gD$, wherein f is 0 or 1, g is 0 or 1 and D is a cyclic group selected from C_{3-g} cycloalkyl group, an aryl group or a 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halp or C1-4alkyl;

group (6) is -R^dR⁴¹; wherein R⁴¹ is a 4-6-membered cycloalkyl or saturated heterocyclic ring, linked via carbon or nitrogen with 1-2 heteroatoms selected independently from O, S and N, which cycloalkyl or heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, Application No. Reply to Office Action of

10/088,852 27th June 2005 28th November 2005

halogeno, cyano, C₁₄alkyl, hydroxyl∑₁₄alkyl, cyanoC₁₄alkyl, cyclopropyl, C_{1-4} alkylsulphonyl C_{1-4} alkyl, C_{1-4} alko:(ycarbonyl, carboxamido, C_{1-4} aminoalkyl, C_{1-4} alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkylaminoC₁₋₄alkyl, C₁₋₄alkanoyl, di(C₁₋₄alkyl)aminoC₁₋₄alkyl, C₁₋₄alkylaminoC₁₋₄alkoxy, di(C₁₋₄alkyl)aminoC₁₋₄alkoxy nitro, amino, C₁₋₄alkoxy, C₁₋₄hydroxyalkoxy, carboxy, trifluor methyl, -C(O)NR⁴³R⁴⁴, -NR⁴⁵C(O)R⁴⁶ wherein R⁴³, R⁴⁴, R⁴⁵ and R⁴⁶ which may be the same or different, each represents hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl, and a group -(-O-)_f(C₁₋₄alkyl)_oringD, wherein f is 0 or 1, g is 0 or 1 and D is a cyclic group se ected from C₃₋₆cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C14alkyl; group (10) is -R⁹R⁴² wherein R⁴² represents a phenyl group or a 5-6-membered aromatic heterocyclic group, linked via carbon or nitrogen, with 1-3 heteroatoms selected from O, N and S, which phenyl or aromatic heterocyclic group may carry up to 5 substituents selected from hydroxy, nitro, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, oxo, cyanoC₁₋₄alkyl, cyclopropyl, C₁₋₄alkylsulphonylC₁₋₄alkyl, C_{14} alkoxycarbonyl, di $(C_{14}$ alkyl)arnino, C_{14} alkylamino C_{14} alkyl, C_{14} alkanoyl, $\underline{\text{di}(C_{14}\text{alkyl})\text{amino}C_{14}\text{alkyl},\ C_{14}\text{alkyl}\text{amino}C_{14}\text{alkoxy},\ \underline{\text{di}(C_{14}\text{alkyl})\text{amino}C_{14}\text{alkoxy},\ \underline{\text{carboxy}},}$ carboxamido, trifluoromethyl, cyano, -C(O)NR⁶⁹R⁷⁰, -NR⁷¹C(O)R⁷², wherein R⁶⁹, R⁷⁰, R⁷¹ and R⁷², which may be the same or different, each represents hydrogen, C1-alkyl, hydroxyC1-alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and a group $-(-O-)_0(C_{1-4}$ alkyl) gring D wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from C₃₋₆cycloalkyl, arvl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C14alkyl; and R^b, R^b, R^d and R^g are independently selected from C₁₋₈alkylene groups optionally substituted by one or more substituents selected from hydroxy, halogeno, amino..

- (currently amended) A compound according to claim 16, or a salt or phosphate ester thereof, wherein R² and R³ are independently methoxy or 3,3,3-trifluoroethoxy.
- (currently amended) A compound according to claim 16, or a salt or phosphate ester 20. thereof, wherein R3 is 3-morpholinopropoxy.
- (currently amended) A compound according to claim 16, or a salt or phosphate ester 21. thereof, wherein R8 and R9 are both hydrogen.

10/088,852 27th June 2005 28th November 2005

- (currently amended) A compound according to claim 16, or a salt or phosphate ester 22. thereof, wherein R⁶ and R⁷ are both hydrogen.
- (new) A compound according to claim 1 or a salt or phosphate ester thereof wherein X is 23. NH or O.
- (new) A compound according to claim 1 or a salt or phosphate ester thereof wherein R⁶ 24. and R⁷ are independently hydrogen or C₁₄alkyl.
- (new) A compound according to claim 1 or a salt or phosphate ester thereof wherein R8 and R⁹ are independently hydrogen, halo, C₁₄alkoxy, cyano, trifluoromethyl or phenyl.

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

□ BLACK BORDERS
□ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
□ FADED TEXT OR DRAWING
□ BLURRED OR ILLEGIBLE TEXT OR DRAWING
□ SKEWED/SLANTED IMAGES
□ COLOR OR BLACK AND WHITE PHOTOGRAPHS
□ GRAY SCALE DOCUMENTS
□ GRAY SCALE DOCUMENTS
□ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

IMAGES ARE BEST AVAILABLE COPY.

OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.